Supplementary data

Figure S1. Distribution and interpretation of *Enterobacterales* isolates in 4,037 patients defined by the pre-2019 and 2019 CLSI breakpoints. LEV, levofloxacin.

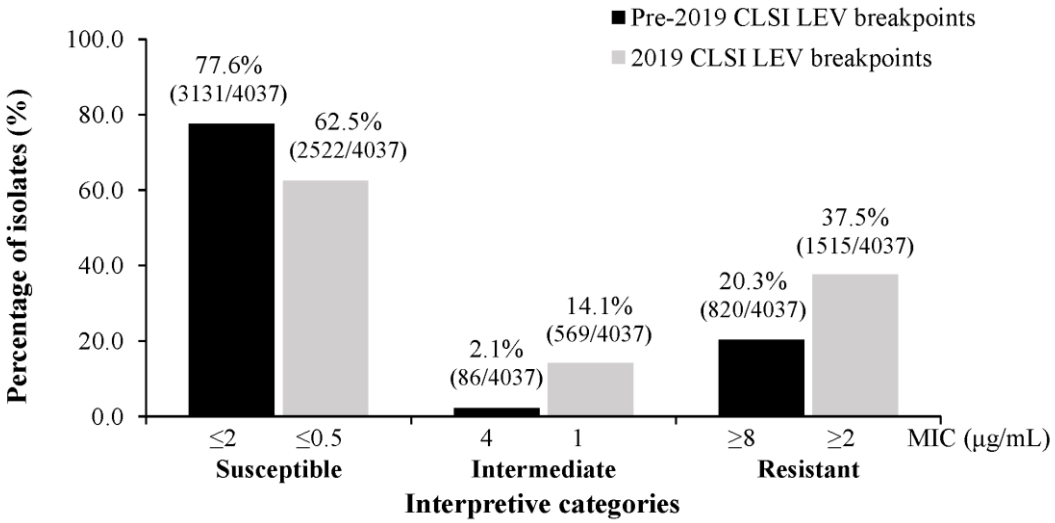

Figure S2. Correlation of levofloxacin resistance and consumption in *Enterobacterales* isolates during the study period according to the pre-2019 or 2019 CLSI breakpoints. Percentage of levofloxacin-resistant *Enterobacterales* isolates (lines) and levofloxacin consumption in DDD per 1000 patient-days (bars). LEV, levofloxacin; DDD, defined daily dose.

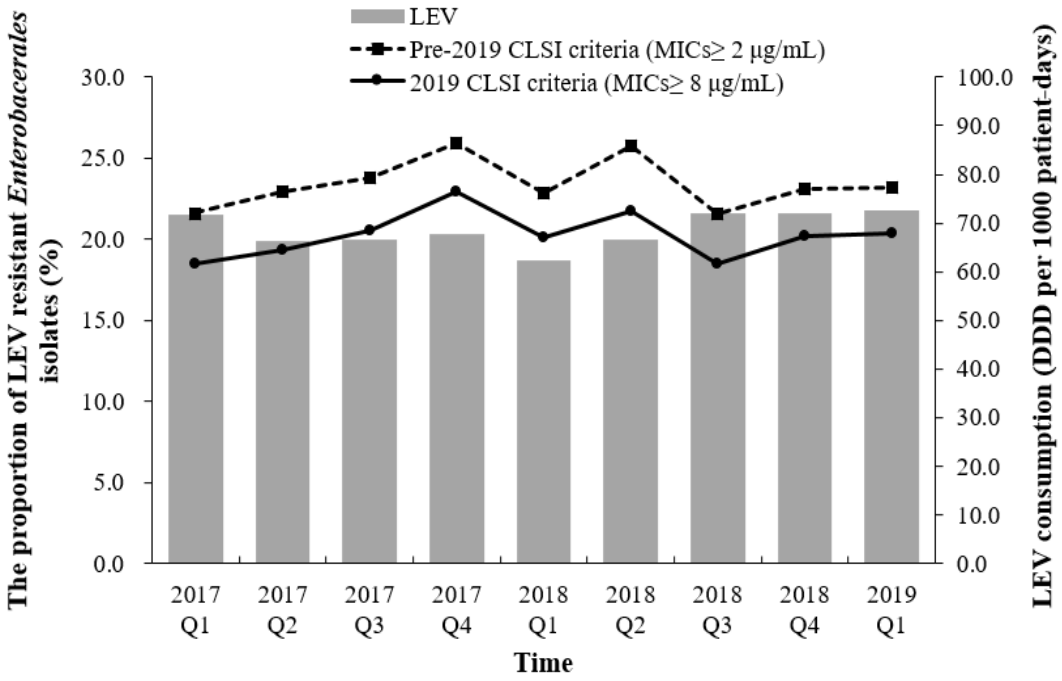

Table S1. Baseline characteristics and outcome of 181 patients after 1:3 propensity score matching [a].

Characteristic	Matched patients n=181, (%)	Levofloxacin MIC (μ g/mL)		*P* value [d]	SMD [e]
		Low-MIC (≤ 0.5) n=130, (%)	High-MIC (1 or 2) n=51, (%)		
Demographics					
Age, yr (mean ± SD)	66.60 ± 14.42	67.13 ± 14.66	65.24 ± 13.84	0.356	-0.137
Sex, male	70 (38.7)	50 (38.5)	20 (39.2)	1.000	0.015
Comorbidities					
Cardiovascular disease	114 (63.0)	80 (61.5)	34 (66.7)	0.453	0.108
Chronic pulmonary disease	8 (4.4)	6 (4.6)	2 (3.9)	0.844	-0.035
Chronic liver disease	9 (5.0)	5 (3.8)	4 (7.8)	0.282	0.147
Chronic renal disease	16 (8.8)	11 (8.5)	5 (9.8)	0.926	0.045
Diabetes	68 (37.6)	46 (35.4)	22 (43.1)	0.421	0.155
Malignancy	58 (32.0)	43 (33.1)	15 (29.4)	0.434	-0.080
Immunocompromised status	15 (8.3)	10 (7.7)	5 (9.8)	0.841	0.070
CCI ≥3	73 (40.3)	49 (37.7)	24 (47.1)	0.486	0.186
Clinical severity					
ICU admission	24 (13.3)	17 (13.1)	7 (13.7)	0.823	0.019
SOFA score ≥5	32 (17.7)	24 (18.5)	8 (15.7)	0.445	-0.076
Pitt bacteremia score ≥4	12 (6.6)	9 (6.9)	3 (5.9)	0.474	-0.044
Hospital-acquired	48 (26.5)	32 (24.6)	16 (31.4)	0.877	0.144
Source of bacteremia					
Pneumonia	15 (8.3)	11 (8.5)	4 (7.8)	0.717	-0.023
Intra-abdominal	23 (12.7)	18 (13.8)	5 (9.8)	0.545	-0.135
Urinary tract	129 (71.3)	91 (70.0)	38 (74.5)	0.456	0.102
Skin and soft tissue	3 (1.7)	2 (1.5)	1 (2.0)	0.918	0.030
Catheter related	7 (3.9)	5 (3.8)	2 (3.9)	1.000	0.004
Others[b]	4 (2.2)	3 (2.3)	1 (2.0)	0.925	-0.025
Organism					
Escherichia coli	125 (69.1)	88 (67.7)	37 (72.5)	0.583	0.108
Enterobacter spp.	13 (7.2)	10 (7.7)	3 (5.9)	0.635	-0.076
Klebsiella spp.	29 (16.0)	20 (15.4)	9 (17.6)	0.485	0.059
Citrobacter spp.	5 (2.8)	5 (3.8)	0 (0.0)	0.420	-
Proteus spp.	3 (1.7)	2 (1.5)	1 (2.0)	0.708	0.030
Serratia marcescens	6 (3.3)	5 (3.8)	1 (2.0)	0.508	-0.135
Empiric therapy				0.798	
Levofloxacin	72 (39.8)	52 (40.0)	20 (39.2)		-0.016

Nonactive antibiotic	45 (24.9)	30 (23.1)	15 (29.4)		0.144
Active antibiotic	64 (35.4)	48 (36.9)	16 (31.4)		-0.116
Levofloxacin therapy				0.640	
750mg	111 (61.3)	82 (63.1)	29 (56.9)		-0.124
500mg	70 (38.7)	48 (36.9)	22 (43.1)		0.124
Source control [c]	48 (26.5)	38 (29.2)	10 (19.6)	0.166	-0.240
Outcome					
30-day mortality	8 (4.4)	2 (1.5)	6 (11.8)	0.043	

SMD, standardized mean difference; CCI, Charlson comorbidity index; ICU, intensive care unit; SOFA, sequential organ failure assessment.

[a] Four pairs matched on case:control ratio of 1:1 and 15 pairs matched on case:control ratio of 1:2.

[b] Other sources included central nervous system (one patient) and unknown source (three patients).

[c] Source control was defined as a removable focus or resolution.

[d] The *P* value was estimated by using conditional logistic regression.

[e] The matching was considered as balanced as SMD were smaller than 0.25.

Figure S3. Proportion of mortality according to target attainment of estimated levofloxacin AUC/MIC of ≥110. AUC/MIC, ratio of area under the concentration-time curve to MIC.